CLAIMS

What is claimed is:

1. A method of increasing cytosolic Ca^{2+} levels in an airway epithelial cell comprising contacting P2X receptors on the cell with an effective amount of Zn^{2+}.
2. The method of claim 1, wherein the P2X receptors are not contacted with zincum gluconium.
3. The method of claim 1, wherein the Zn^{2+} is in the form of zinc chloride.
4. The method of claim 1 further comprising contacting the cell with an effective amount of ATP.
5. The method of claim 1, further comprising alkalinizing the cell's extracellular fluid or contacting the cell with an alkalinized solution containing Zn^{2+}.
6. The method of claim 5, wherein the alkalinized solution has a pH of about 7.7-8.1.
7. The method of claim 6, wherein the alkalinized solution has a pH of about 7.8-7.9.
8. The method of claim 1, further comprising reducing the cell's extracellular Na+ or contacting the cell with a Zn^{2+} containing solution with low Na+ .
9. The method of claim 1, further comprising reducing the cell's extracellular Mg^{2+} or contacting the cell with a Zn^{2+} containing solution with low Mg^{2+}.
10. The method of claim 1, further comprising increasing the cell's extracellular Ca^{2+} or contacting the cell with a Zn^{2+} containing solution with high Ca^{2+}.
11. The method of claim 10, wherein the cell's extracellular Ca^{2+} or the Ca^{2+} level of the solution is increased by 1.5-3 mM over basal levels.
12. The method of claim 1, further comprising
    (a) contacting the cell with an effective amount of ATP,
    (b) reducing the cell's extracellular Na+ or contacting the cell with a Zn^{2+} containing solution with low Na+,

(c) alkalinizing the cell's extracellular fluid or contacting the cell with an alkaline solution containing Zn+,

(d) reducing the cell's extracellular Mg^{2+} or contacting the cell with a Zn^{2+} containing solution with low Mg^{2+},

(e) increasing the cell's extracellular Ca^{2+} or contacting the cell with a Zn^{2+} containing solution with high Ca^{2+}, or

(f) any combination of steps a-e.

13. A method of treating an airway disease in a subject, comprising contacting epithelial cells in the trachea, bronchi, bronchioles, or alveoli of a subject with an effective amount of Zn^{2+}.

14. The method of claim 13, further comprising reducing the cell's extracellular Na^{+} or contacting the cell with a Zn^{2+} containing solution with low Na^{+}.

15. The method of claim 13, further comprising reducing the cell's extracellular Mg^{2+} or contacting the cell with a Zn^{2+} containing solution with low Mg^{2+}.

16. The method of claim 13, further comprising increasing the cell's extracellular Ca^{2+} or contacting the cell with a Zn^{2+} containing solution with high Ca^{2+}.

17. The method of claim 16, wherein the cell's extracellular Ca^{2+} or the level of Ca^{2+} in the Zn+ containing solution is increased by 1.5-3 mM over basal levels.

18. The method of claim 13, further comprising alkalinizing the cell's extracellular fluid or contacting the cell with an alkalinized solution containing Zn^{2+}.

19. The method of claim 18, wherein the extracellular solution or the alkalinized solution has a pH of about 7.7-8.1.

20. The method of claim 19, wherein the extracellular solution or the alkalinized solution has a pH of about 7.8-7.9.

21. The method of claim 13, further comprising

(a) contacting the cell with an effective amount of ATP,

(b) reducing the cell's extracellular Na+ or contacting the cell with a Zn^{2+} containing solution with low Na+,

(c) alkalinizing the cell's extracellular fluid or contacting the cell with an alkaline solution containing Zn+,

(d) reducing the cell's extracellular Mg^{2+} or contacting the cell with a Zn^{2+} containing solution with low Mg^{2+},

(e) increasing the cell's extracellular Ca^{2+} or contacting the cell with a Zn^{2+} containing solution with high Ca^{2+}, or

(f) any combination of steps a-e.

22. The method of claim 13, wherein the contacting step is performed with an Zn^{2+}-containing inhalant, nebulization, aerosol, or instillant.

23. The method of claim 13, wherein the zinc is in the form of zinc chloride ($ZnCl_2$).

24. A method of treating airway disease in a subject, comprising contacting the subject's airway epithelial cells with an alkaline composition comprising an effective amount of a P2X receptor agonist.

25. The method of claim 24, wherein the agonist is Zn^{2+}.

26. The method of claim 24, wherein the agonist is ATP.

27. The method of claim 24, further comprising reducing the cell's extracellular Na+ or reducing Na+ levels in the composition.

28. The method of claim 24, further comprising reducing the cell's extracellular Mg^{2+} or reducing Mg^{2+} levels in the composition.

29. The method of claim 24, further comprising increasing the cell's extracellular Ca^{2+} or increasing Ca^{2+} levels in the composition.

30. The method of claim 29, wherein the cell's extracellular Ca^{2+} or Ca^{2+} level in the compositon is increased by 1.5-3 mM over basal levels.

31. The method of claim 24, wherein the P2X receptor agonist is Zn^{2+}.

32. The method of claim 24, wherein the alkalinized solution has a pH of about 7.7-8.1.

33. The method of claim 32, wherein the alkalinized solution has a pH of about 7.8-7.9.

34. The method of claim 24, further comprising

(a) contacting the cell with an effective amount of ATP,

(b) reducing the cell's extracellular Na+ or contacting the cell with a Zn^{2+} containing solution with low Na+,

(c) alkalinizing the cell's extracellular fluid or contacting the cell with an alkaline solution containing Zn+,

(d) reducing the cell's extracellular Mg^{2+} or contacting the cell with a Zn^{2+} containing solution with low Mg^{2+},

(e) increasing the cell's extracellular Ca^{2+} or contacting the cell with a Zn^{2+} containing solution with high Ca^{2+}, or

(f) any combination of steps a-e.

35. The method of claim 24, wherein the contacting step is performed with an Zn^{2+}-containing inhalant, nebulization, aerosol, or instillant.

36. The method of claim 24, wherein the zinc is in the form of zinc chloride ($ZnCl_2$).

37. A composition comprising zinc and a saline solution, wherein the saline solution has low Na+, is enriched with Ca^{2+}, and is modified to an alkaline pH.

38. A nasal spray comprising the composition of claim 37.

39. A nebulizer comprising the composition of claim 37.

40. An aerosol inhaler comprising the composition of claim 37.

41. The composition of claim 37, wherein the zinc is not in the form of zincum gluconium.

42. A method of treating a bacterial infection in a subject, comprising administering to the subject the composition of claim 37.

43. A method of reducing inflammation in a subject, comprising administering to the subject the composition of claim 37.

44. A method of treating polycystic kidney disease in a subject, comprising administering to the subject the composition of claim 37.

45. A method of treating a subject with an endocrine disorder, comprising administering to the subject the composition of claim 37.

46. The method of claim 45, wherein the endocrine disorder is a "failure to secrete agonist" disorder.

47. The method of claim 46, wherein the "failure to secrete agonist" disorder is diabetes.

48. A method of screening for an airway epithelial Ca^{2+} entry channel agonist, comprising

(a) contacting an airway epithelial cell with a test compound;

(b) detecting calcium levels in the airway epithelial cell; and

(c) screening for a sustained elevation in calcium as compared to a control level, indicating an airway epithelial Ca^{2+} entry channel agonist.

49. The method of claim 48, wherein the Ca^{2+} entry channel is selected from the group consisting of a P2X purinergic receptor Ca^{2+} entry channel, a transient receptor potential (TRP) Ca^{2+} entry channel, a store-operated Ca^{2+} (SOC) entry channel, a calcium release activated channel (ICRAC), and a CAT-1 Ca^{2+} entry channel.

50. The method of claim 48, further comprising the step of:

(d) screening for reversibility of response by removing the agonist during the assay.

51. The method of claim 50, further comprising the step of:

(e) screening for dependence upon extracellular Ca^{2+} by repeating the assay in a solution devoid of extracellular Ca^{2+}.

52. The method of claim 48, wherein the airway epithelial cell is a cystic fibrosis airway epithelial cell.

53. The method of claim 52, wherein the cystic fibrosis airway epithelial cell is selected from the group consisting of an IB3-1 human CF bronchial

epithelial cell line, a CFBE41o- human bronchial epithelial cell line, and a CFPAC-1 cell line.

54. The method of claim 48, wherein the calcium levels are detected using a calcium indicator.

55. The method of claim 48, wherein the airway epithelial cell is in a low Na+ solution.

56. The method of claim 48, wherein the airway epithelial cell is in a 0 Na+ solution.

57. The method of claim 48, wherein the airway epithelial cell is in a Ca^{2+}-enriched solution.

58. The method of claim 48, wherein the airway epithelial cell is in a solution containing an effective amount of ATP.

59. The method of claim 58, wherein the amount of ATP is about 1 to about 500 micromolar.

60. The method of claim 59, wherein the amount of ATP is about 10 to about 200 micromolar.

61. The method of claim 48, wherein the airway epithelial cell is in a solution containing an effective amount of zinc.

62. The method of claim 61, wherein the amount of zinc is about 1 to about 100 micromolar.

63. The method of claim 62, wherein the amount of zinc is about 10 to about 50 micromolar.

64. The method of claim 48, wherein the airway epithelial cell is in an alkaline solution.

65. The method of claim 64, wherein the alkaline solution has a pH of about 7.6-8.0.

66. The method of claim 65, wherein the alkaline solution has a pH of about 7.8-7.9.

67. The method of claim 66, wherein the alkaline solution has a pH of about 7.8.

68. The method of claim 48, wherein the airway epithelial cell is in a 0 Mg^{2+} solution.

69. The method of claim 48, wherein the airway epithelial cell is in a low Mg^{2+} solution.

70. A method of screening for an airway epithelial Ca^{2+} entry channel agonist, comprising

(a) contacting a first airway epithelial cell with more than one test compound;

(b) detecting calcium levels in the first airway epithelial cell;

(c) selecting each of test compounds in the group that contacted the first airway epithelial cell, wherein the first airway epithelial cell showed a sustained elevation in calcium;

(d) contacting a second airway epithelial cell with one test compound selected in step (c); and

(e) detecting calcium levels in the second airway epithelial cell, a sustained elevation in calcium as compared to a control level, indicating an airway epithelial Ca^{2+} entry channel agonist.

71. The method of claim 70, wherein the Ca^{2+} entry channel is selected from the group consisting of a P2X purinergic receptor Ca^{2+} entry channel, a transient receptor potential (TRP) Ca^{2+} entry channel, a store-operated Ca^{2+} (SOC) entry channel, a calcium release activated channel (ICRAC), and a CAT-1 Ca^{2+} entry channel.

72. The method of claim 70, further comprising

(f) screening for reversibility of response by removing the agonist during the assay.

73. The method of claim 72, further comprising

(g) screening for dependence upon extracellular Ca^{2+} by repeating the assay in a solution devoid of extracellular Ca^{2+}.

74. The method of claim 70, wherein the airway epithelial cell is a cystic fibrosis airway epithelial cell.

75. The method of claim 74, wherein the cystic fibrosis airway epithelial cell is selected from the group consisting of an IB3-1 human CF bronchial epithelial cell line, a CFBE41o- human bronchial epithelial cell line, and a CFPAC-1 cell line.

76. The method of claim 70, wherein the calcium levels are detected using a calcium indicator.

77. The method of claim 70, wherein the airway epithelial cell is in a low Na+ solution.

78. The method of claim 70, wherein the airway epithelial cell is in a 0 Na+ solution.

79. The method of claim 70, wherein the airway epithelial cell is in a Ca^{2+}-enriched solution.

80. The method of claim 70, wherein the airway epithelial cell is in a solution containing an effective amount of ATP.

81. The method of claim 80, wherein the amount of ATP is about 1 to about 500 micromolar.

82. The method of claim 81, wherein the amount of ATP is about 10 to about 200 micromolar.

83. The method of claim 70, wherein the airway epithelial cell is in a solution containing an effective amount of zinc.

84. The method of claim 83, wherein the amount of zinc is about 1 to about 100 micromolar.

85. The method of claim 84, wherein the amount of zinc is about 10 to about 50 micromolar.

86. The method of claim 70, wherein the airway epithelial cell is in an alkaline solution.

87. The method of claim 86, wherein the alkaline solution has a pH of about 7.6-8.0.

88. The method of claim 87, wherein the alkaline solution has a pH of about 7.8-7.9.

89. The method of claim 88, wherein the alkaline solution has a pH of about 7.8.

90. The method of claim 70, wherein the airway epithelial cell is in a low Mg^{2+} solution.

91. The method of claim 70, wherein the airway epithelial cell is in a 0 Mg^{2+} solution.

92. A method of screening for a Ca^{2+} entry channel agonist, comprising

(a) contacting a test compound with a cell that expresses a heterologous nucleic acid that encodes a Ca^{2+} entry channel receptor; and

(b) detecting calcium levels in the cell;

sustained elevation in calcium as compared to a control level, indicating a Ca^{2+} entry channel agonist

93. The method of claim 92, wherein the Ca^{2+} entry channel is selected from the group consisting of a P2X purinergic receptor Ca^{2+} entry channel, a transient receptor potential (TRP) Ca^{2+} entry channel, a store-operated Ca^{2+} (SOC) entry channel, a calcium release activated channel (ICRAC), and a CAT-1 Ca^{2+} entry channel.

94. The method of claim 92, further comprising

(c) screening for reversibility of response by removing the agonist during the assay.

95. The method of claim 94, further comprising

(d) screening for dependence upon extracellular Ca^{2+} by repeating the assay in a solution devoid of extracellular Ca^{2+}.

96. The method of claim 92, wherein the heterologous nucleic acid encodes a receptor selected from the group consisting of a P2X4 receptor, a P2X5 receptor, and a P2X6 receptor.

97. The method of claim 92, wherein the airway epithelial cell is a cystic fibrosis airway epithelial cell.

98. The method of claim 92, wherein the calcium levels are detected using a calcium indicator.

99. The method of claim 92, wherein the airway epithelial cell is in a low Na+ solution.

100. The method of claim 92, wherein the airway epithelial cell is in a 0 Na+ solution.

101. The method of claim 92, wherein the airway epithelial cell is in a Ca^{2+}-enriched solution.

102. The method of claim 92, wherein the airway epithelial cell is in a solution containing an effective amount of ATP.

103. The method of claim 102, wherein the amount of ATP is about 1 to about 500 micromolar.

104. The method of claim 103, wherein the amount of ATP is about 10 to about 200 micromolar.

105. The method of claim 92, wherein the airway epithelial cell is in a solution containing an effective amount of zinc.

106. The method of claim 105, wherein the amount of zinc is about 1 to about 100 micromolar.

107. The method of claim 106, wherein the amount of zinc is about 10 to about 50 micromolar.

108. The method of claim 92, wherein the airway epithelial cell is in an alkaline solution.

109. The method of claim 108, wherein the alkaline solution has a pH of about 7.6-8.0.

110. The method of claim 109, wherein the alkaline solution has a pH of about 7.8-7.9.

111. The method of claim 110, wherein the alkaline solution has a pH of about 7.8.

112. The method of claim 92, wherein the airway epithelial cell is in a low Mg^{2+} solution.

113. The method of claim 92, wherein the airway epithelial cell is in a 0 Mg^{2+} solution.

114. A method of screening for a gastrointestinal epithelial Ca^{2+} entry channel agonist, comprising:

(a) contacting a gastrointestinal epithelial cell with a test compound; and

(b) Detecting calcium levels in the gastrointestinal epithelial cell; a sustained elevation in calcium as compared to a control level, indicating the gastrointestinal epithelial Ca^{2+} entry channel agonist.

115. The method of claim 114, wherein the Ca^{2+} entry channel is selected from the group consisting of a P2X purinergic receptor Ca^{2+} entry channel, a transient receptor potential (TRP) Ca^{2+} entry channel, a store-operated Ca^{2+} (SOC) entry channel, a calcium release activated channel (ICRAC), and a CAT-1 Ca^{2+} entry channel.

116. The method of claim 114, further comprising

(c) screening for reversibility of response by removing the agonists during the assay.

117. The method of claim 116, further comprising

(d) screening for dependence upon extracellular Ca^{2+} by repeating the assay in solution devoid of extracellular Ca^{2+}.

118. The method of claim 114, wherein the gastrointestinal epithelial cell is a cystic fibrosis pancreatic epithelial cell.

119. The method of claim 118, wherein the cystic fibrosis gastrointestinal epithelial cell is a CFPAC CF human pancreatic epithelial cell line.

120. The method of claim 114, wherein the calcium levels are detected using a calcium indicator.

121. The method of claim 114, wherein the gastrointestinal epithelial cell is in a low Na+ solution.

122. The method of claim 114, wherein the gastrointestincal epithelial cell is in a 0 Na+ solution.

123. The method of claim 114, wherein the gastrointestinal epithelial cell is in a Ca^{2+}-enriched solution.

124. The method of claim 114, wherein the gastrointestinal epithelial cell is in a solution containing an effective amount of ATP.

125. The method of claim 124, wherein the amount of ATP is about 1 to about 500 micromolar.

126. The method of claim 125, wherein the amount of ATP is about 10 to about 200 micromolar.

127. The method of claim 114, wherein the gastrointestinal epithelial cell is in a solution containing an effective amount of zinc.

128. The method of claim 127, wherein the amount of zinc is about 1 to about 100 micromolar.

129. The method of claim 128, wherein the amount of zinc is about 10 to about 50 micromolar.

130. The method of claim 114, wherein the gastrointestinal epithelial cell is in an alkaline solution.

131. The method of claim 130, wherein the alkaline solution has a pH of about 7.6-8.0.

132. The method of claim 131, wherein the alkaline solution has a pH of about 7.8-7.9.

133. The method of claim 132, wherein the alkaline solution has a pH of about 7.8.

134. The method of claim 114, wherein the gastrointestinal epithelial cell is in a low Mg^{2+} solution.

135. The method of claim 114, wherein the gastrointestinal epithelial cell is in a 0 Mg^{2+} solution.

136. A method of treating polycystic kidney disease (PKD) in a subject, comprising administering to the subject an effective amount of Zn^{2+}.

137. The method of claim 136, wherein the effective amount of zinc is in the range of 10-100 μM.

138. A method of treating a subject with an endocrine disorder comprising administering to the subject an effective amount of Zn^{2+}.

139. The method of claim 138, wherein the endocrine disorder is a "failure to secrete agonist" disorder.

140. The method of claim 138, wherein the effective amount of zinc is in the range of 10-100 μM.

141. The method of claim 139, wherein the "failure to secrete agonist" disorder is diabetes.